

**AMENDMENTS TO THE CLAIMS:**

Amend the claims as follows:

1. (Original) An isolated HBV polynucleic acid or a fragment thereof, said polynucleic acid or said fragment characterized in that it comprises codon 204 of the HBV reverse transcriptase domain wherein said codon 204 is encoding a serine.

2. (Original) The HBV polynucleic acid or fragment thereof according to claim 1, said polynucleic acid or fragment further characterized in that it comprises codon 180 of the HBV reverse transcriptase domain wherein said codon 180 is encoding a methionine.

3. (Currently Amended) The HBV polynucleic acid or fragment thereof according to claim 1 which is defined by SEQ ID NO:6 or the complement thereof, ~~or said fragment according to claims 1 or 2 which is derived from SEQ ID NO:6 or the complement thereof.~~

4. (Original) An isolated HBV DNA polymerase/reverse transcriptase protein or a fragment thereof, said protein or fragment characterized in that it comprises amino acid 204 of the HBV reverse transcriptase domain and wherein said amino acid 204 is a serine.

5. (Original) The HBV DNA polymerase/reverse transcriptase protein or fragment thereof according to claim 4 characterized further in that it comprises amino acid 180 of the HBV reverse transcriptase domain and wherein said amino acid 180 is a methionine.

6. (Currently Amended) An isolated HBV DNA polymerase/reverse transcriptase protein or a fragment thereof, said protein or fragment characterized in that it comprises

amino acid 204 of the HBV reverse transcriptase domain and wherein said amino acid

204 is a serine, said protein or fragment thereof being ~~The HBV DNA~~

~~polymerase/reverse transcriptase protein or fragment thereof according to claim 4 which~~  
~~is encoded by the isolated HBV polynucleic acid or fragment thereof according to [[any]]~~  
one of claims 1 to 3.

7. (Previously Presented) The HBV DNA polymerase/reverse transcriptase protein or fragment thereof according to claim 4 which is defined by SEQ ID NO:4, or a fragment thereof.

8. (Currently Amended) An isolated [[HBV variant]]variant Hepatitis B virus comprising a polynucleic acid or fragment thereof according to claim 1.

9. (Currently Amended) An isolated [[HBV variant]]variant Hepatitis B virus comprising a protein or fragment thereof according to claim 4.

10. (Previously Presented) A vector comprising the HBV polynucleic acid or fragment thereof according to claim 1.

11. (Currently Amended) A host cell comprising the HBV polynucleic acid or fragment thereof according to claim 1, an [[HBV variant]]variant Hepatitis B virus containing said polynucleic acid or fragment thereof or a vector containing said polynucleic acid or fragment thereof.

12. (Currently Amended) A host cell comprising the HBV DNA polymerase/reverse transcriptase protein or fragment thereof according to claim 4 or an [[HBV variant]]variant Hepatitis B virus containing said HBV DNA polymerase/reverse transcriptase protein or fragment thereof.

13. (Previously Presented) A method for detecting the presence of a HBV in a biological sample, said method comprising the step of detecting the presence of a HBV polynucleic acid or fragment thereof according to claim 1.

14. (Original) The method according to claim 13 comprising:

(i) obtaining a target HBV polynucleic acid from said biological sample wherein said target HBV polynucleic acid is suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;

(ii) obtaining the nucleic acid sequence of the target HBV polynucleic acid of (i);

(iii) inferring, from the nucleic acid sequence obtained in (ii), the presence of said serine-encoding codon 204 of the HBV reverse transcriptase domain or of said methionine-encoding codon 180 and said serine-encoding codon 204 of the HBV reverse transcriptase domain and, therefrom, the presence of said HBV in said biological sample.

15. (Currently Amended) The method according to claims 13 comprising:

(i) obtaining a target HBV polynucleic acid from said biological sample wherein said target HBV polynucleic acid is suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;

(ii) contacting the target HBV polynucleic acid of (i) with an oligonucleotide capable of discriminating a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine resulting in a discriminatory signal relating to codon 204,

or with an oligonucleotide capable of discriminating a codon 180 encoding a methionine from a codon 180 encoding a leucine resulting in a discriminatory signal relating to codon 180 and an oligonucleotide capable of discriminating a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine resulting in a discriminatory signal relating to codon 204;

(iii) inferring, from the discriminatory signal obtained in (ii), the presence of said serine-encoding codon 204 of the HBV reverse transcriptase or of said discriminatory signals relating to codon 204 and to codon 180 obtained in (ii) of said methionine-encoding codon 180 and said serine-encoding codon 204 of the HBV reverse transcriptase domain and, therefrom, the presence of said HBV in said biological sample.

16. (Original) The method according to claim 15 wherein said discriminating in (ii) is based on hybridization and wherein said discriminatory signal in (iii) is a hybridization signal.

17. (Previously Presented) A method for detecting resistance to an antiviral drug of a HBV virus present in a biological sample, said method comprising the step of detecting the presence of a HBV polynucleic acid or fragment thereof according to claim 1.

18. (Original) The method according to claim 17 comprising:

- (i) obtaining a target HBV polynucleic acid from said biological sample wherein said target HBV polynucleic acid is suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;
- (ii) obtaining the nucleic acid sequence of the target HBV polynucleic acid of (i);
- (iii) inferring, from the nucleic acid sequence obtained in (ii), the presence of said serine-encoding codon 204 in the HBV reverse transcriptase domain or of said methionine-encoding codon 180 and said serine-encoding codon 204 in the HBV reverse transcriptase domain and, therefrom, said resistance to an antiviral drug of a HBV virus present in said biological sample.

19. (Currently Amended) The method according to claim 17 comprising:

- (i) obtaining a target HBV polynucleic acid from said biological sample wherein said target HBV polynucleic acid is suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;
- (ii) contacting the target HBV polynucleic acid of (i) with an oligonucleotide capable of discriminating a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine resulting in a discriminatory signal relating to codon 204.

or with an oligonucleotide capable of discriminating a codon 180 encoding a methionine from a codon 180 encoding a leucine resulting in a discriminatory signal relating to codon 180 and an oligonucleotide capable of discriminating a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine resulting in a discriminatory signal relating to codon 204;

(iii) inferring, from the discriminatory signal obtained in (ii), the presence of said serine-encoding codon 204 in the HBV reverse transcriptase domain or of said discriminatory signals relating to codon 204 and to codon 180 obtained in (ii) of said methionine-encoding codon 180 and said serine-encoding codon 204 in the HBV reverse transcriptase domain and, therefrom, said resistance to an antiviral drug of a HBV virus present in said biological sample.

20. (Original) The method according to claim 19 wherein said discriminating in (ii) is based on hybridization and wherein said discriminatory signal in (iii) is a hybridization signal.

21. (Previously Presented) A diagnostic kit for detecting the presence of a HBV in a biological sample, said kit comprising a means for detecting the presence of a HBV polynucleic acid or fragment thereof according to claim 1.

22. (Original) The diagnostic kit according to claim 21 comprising:

(i) optionally, a means for obtaining the nucleic acid sequence of a target HBV polynucleic acid suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;

(ii) a means for inferring, from the nucleic acid sequence obtained in (i), the presence of said serine-encoding codon 204 of the HBV reverse transcriptase domain or of said methionine-encoding codon 180 and said serine-encoding codon 204 of the HBV reverse transcriptase domain and, therefrom, the presence in said biological sample of said HBV.

23. (Original) The diagnostic kit according to claim 21 comprising an oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine.

24. (Original) The diagnostic kit according to claim 23 further comprising an oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 180 encoding a methionine from a codon 180 encoding a leucine.

25. (Previously Presented) A diagnostic kit for detecting resistance to an antiviral drug of a HBV virus present in a biological sample, said kit comprising a means for detecting the presence of a HBV polynucleic acid or fragment thereof according to claim 1.

26. (Original) The diagnostic kit according to claim 25 comprising:

(i) optionally, a means for obtaining the nucleic acid sequence of the target HBV polynucleic acid suspected to comprise a serine-encoding codon 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon 180 and a serine-encoding codon 204 of the HBV reverse transcriptase domain;

(ii) a means for inferring, from the nucleic acid sequence obtained in (i), the presence of said serine-encoding codon 204 in the HBV reverse transcriptase domain or of said methionine-encoding codon 180 and said serine-encoding codon 204 in the

HBV reverse transcriptase domain and, therefrom, resistance to an antiviral drug of a HBV virus present in said biological sample.

27. (Original) The diagnostic kit according to claim 25 comprising an oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine.

28. (Original) The diagnostic kit according to claim 27 further comprising an oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 180 encoding a methionine from a codon 180 encoding a leucine.

29. (Currently Amended) The diagnostic kit according to claim ~~[[23]]~~27 further comprising a means for detecting ~~[[the]]~~a discriminatory signal obtained by contacting said HBV polynucleic acid and said oligonucleotide ~~or oligonucleotides~~.

30. (Currently Amended) The diagnostic kit according to claim ~~[[23]]~~27 wherein said oligonucleotide ~~or oligonucleotides~~ are attached or immobilized to a solid support.

31. (Withdrawn) A method for detecting resistance to an antiviral drug of a HBV virus present in a biological sample, said method comprising the step of detecting the presence of a HBV DNA polymerase/reverse transcript protein or fragment thereof according to claim 4.

32. (Withdrawn) A method for screening for drugs active against a HBV virus comprising a polynucleic acid according to claim 1 or comprising a protein encoded by said polynucleic acid, said method comprising:

- (i) measuring replication of said HBV virus in the absence of said drug;
- (ii) measuring replication of said HBV virus in the presence of said drug;



(iii) inferring from (i) and (ii) the inhibitory effect of said drug on replication of said HBV virus.

33. (Currently Amended) The method according to claim 32 further comprising performing steps (i), (ii) and (iii) with a wild-type HBV virus and comparing the inhibitory effect of said drug on replication of said wild-type HBV virus with the inhibitory effect of said drug on replication of the HBV virus comprising [[a]] the polynucleic acid [[according to claim 1]] or comprising a DNA polymerase/reverse transcriptase protein encoded by said poynucleic acid.

34. (Withdrawn) A method for screening for drugs active against a HBV virus comprising a polynucleic acid according to claim 1 or comprising a protein encoded by said poynucleic acid, said method comprising:

- (i) measuring a DNA polymerase/reverse transcriptase activity of said HBV virus in the absence of said drug;
- (ii) measuring the same DNA polymerase/reverse transcriptase activity as in (i) of said HBV virus in the presence of said drug;
- (iii) inferring from (i) and (ii) the inhibitory effect of said drug on said DNA polymerase/reverse transcriptase activity of said HBV virus.

35. (Withdrawn) The method according to claim 34 further comprising performing steps (i), (ii) and (iii) with a wild-type HBV virus and comparing the inhibitory effect of said drug on said DNA polymerase/reverse transcriptase activity of said wild-type HBV virus with the inhibitory effect of said drug on said DNA polymerase/reverse transcriptase activity of the HBV virus comprising said polynucleic acid or comprising said DNA polymerase/reverse transcriptase protein.

Claim 36. (Canceled)

37. (Withdrawn) An oligonucleotide capable of discriminating, in a HBV polynucleic acid or fragment thereof according to claim 1, a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine in the HBV reverse transcriptase domain.

38. (new) The diagnostic kit according to claim 28 further comprising a means for detecting a discriminatory signal obtained by contacting said HBV polynucleic acid and said oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine and means for detecting a discriminatory signal obtained by contacting said HBV polynucleic acid and said oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 180 encoding a methionine from a codon 180 encoding a leucine.

39. (new) The diagnostic kit according to claim 28 wherein at least one of said oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 204 encoding a serine from a codon 204 encoding a methionine, valine or isoleucine is attached or immobilized to a solid support and

said oligonucleotide capable of discriminating, in said HBV polynucleic acid, a codon 180 encoding a methionine from a codon 180 encoding a leucine is attached or immobilized to a solid support.